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09/369,992	08/06/1999	ANNA KATE URSULA KARA	64-99	7524

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	29

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/369,992	Kara et al
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 30, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above, claim(s) *12 and 16-45* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11 and 13-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-45* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *8,9*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-45 are pending.

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

2. The information disclosure statements filed February 15, 2000 and February 17, 2000 have been considered.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

4. Please see attached US-PTO 948.

Election/Restriction

5. Applicant's election with traverse of Group I, species SEQ ID No 1, nucleotides 1147-1740 in Paper No. 28 is acknowledged. The traversal is on the ground(s) that the "oligonucleotide as short as 15 nucleotides, such a short molecule would not be likely to be used in making a polypeptide" and that restriction is in error wherein the claims grouped separately cannot constitute a serious burden These arguments have been fully considered but are not found to be persuasive for the reasons below.

It is the position of the examiner that the claims recite the phrase "at least 15 nucleotides" and includes within the scope of the claims, very large polynucleotides that encode complete proteins. The claims as presented utilize nucleotide sequences that encode peptides and polypeptides, as no upper limit, to the size of the probe or primer used in the claimed method, is recited.

With respect to defining serious burden, the following discussion is set forth to show that burden is defined by a number of factors.

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1)independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.1). In the instant situation, the inventions of Groups I-VI are drawn to distinct inventions which are related as separate products - capable of separate functions. Restrictions between the inventions is deemed to be proper for the reason previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of Groups I-VI are classified separately necessitating different searches of issued US Patents. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because for example the nucleotide sequence of one coding sequence is not identical to another coding sequence for a different protein (oxidase enzyme verses ribosomal subunits). Additionally, it is submitted that the inventions of Groups I-VI have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made Final.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 5-11, 13-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description.*

The claims recite the utilization of a probe or primer that comprises at least 15 nucleotides, the at least 15 nucleotide containing probe or primer comprises "a nucleotide sequence that is highly conserved in Plasmodium berghei and said malarial agent of humans". The conserved sequence is not claimed based upon any reference structure defined by a SEQ ID NO (claim 1), and the size of the conserved sequence could be of any length as long as it is conserved.

The genus of probes and primers that comprise any portion of an P.berghei extrachromosomal element, which may be mitochondrial or plastid associated sequence. The probe or primer sequence being one of any number of nucleotides in length, and may be of any sequence that will detect any Plasmodial malarial agent that is be known to share some homology (P.falciparum) or less homology (P.vivax) with P.berghei (see McCutchan et al (1984, reference cited herein, page 809, abstract, top of page "The DNA of Plasmodium vivax, which is also a human parasite, fits into a distinctly different group" from that of P.falciparum and rodent malarial parasite P.berghei.)

As the conserved nucleotide sequence is not structurally defined other than by functional language, the number of nucleotides that defines the conserved portion of the recited probe or primer could be one or more nucleotides in length. The method utilizes a genus of probes and primers that may only contain a common nucleotide and is any length greater than 15 nucleotides

which is able to hybridize to a sequence in a sample or a nucleic acid derived therefrom. The genus of probes and primers utilized in the claimed method have not been described to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed.

Applicants have not described, nor disclosed the claimed genus of methods that utilize the recited genus of probes and primer sequence or complementary sequences which meet the functional limitations of being able to detect a human malarial agent.

The specification does not provide written description support for the recited genus of probes and primer sequences in the instant specification. The skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by

only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The specification fails to provide adequate written description for the claimed genus of probes and primers that share a conserved sequence with SEQ ID NO 1, nucleotides 1147-1740 or with any portion of any extrachromosomal genetic element of P.berghei. The specification does not disclose a representative number of species described by structure, physical or chemical characteristics, function correlated with structure or a combination of these sufficient to establish that the applicant had possession of the genus probes and primers that would detect any human malarial agent and could be used in the claimed method to detect a human malarial agent.

A probe or primer sequence of SEQ ID No 1, nucleotides 1147-1740 does evidence support in the instant specification but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Interim Guidelines on Written Description,.(Fed Reg , June 15, 1998, Volume 63, Number 114, pages 32639-32645)

and the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 defines the probe or primer to be "the extrachromosomal genetic element" from Plasmodium berghei plastid or plastid-like molecule. While it is possible that conserved sequences are present within the coding sequences of the genes the extrachromosomal genetic element carries, the entire extrachromosomal genetic element does not define a highly conserved nucleic acid sequence of all malarial agents of humans. Plasmodium berghei (claim limitations set forth in claim 1, from which claim 2 depends) is a rodent pathogen. The probe or primer of claim 2 is defined to be the detection agent in a biological sample for the detection of a human Plasmodium malarial agent. Claim 2 is not enabled for the detection of human pathogens as Plasmodium berghei is a rodent pathogen and the extrachromosomal genetic element as a whole is not highly conserved in human malarial agents, such as P.vivax which is taught by McCutchan et al (1984, Science) to not be related to P. Berghei . The Plasmodium berghei extrachromosomal genetic element would not be present in Plasmodium vivax, a human malarial agent. Claim 2 is not enabled for the utilization of the extrachromosomal genetic element of

Plasmodium berghei plastid or plastid-like molecule, which contains 35 kb nucleotides (clearly contains at least 15 nucleotides, limitations required by claim 1), as a probe or primer in the detection of a human malarial agent.

The specification does not define Plasmodium berghei as a human pathogen, no naturally occurring human malarial pathogens are disclosed to comprise the extrachromosomal genetic element of Plasmodium berghei, therefore the person of skill in the art would have to carry out undue experimentation to detect human malarial pathogens utilizing the extrachromosomal genetic element of Plasmodium berghei that is not present, nor highly conserved in human plasmodial pathogen agents.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-11, 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 contacts a biological sample with a probe or primer. The source, nature or type of sample is not defined to be a human sample, nor a blood sample, but a biological sample. The type of biological sample would define what would be present in the sample. If the biological sample is not one that would comprise a human malarial agent, a human agent would not be

detected. The invention is not distinctly claimed in light of the biological sample not being so defined as to comprise a human sample.

Claim 1 defines the probe or primer to comprise one or two components, the first being one that is a sequence of the extrachromosomal element of P.berghei

Claims 2-11 and 13-15 depend from claim 1. Claim 1 recites the phrase "or nucleic acid derived therefrom" which refers back to the "sample" , Plasmodium berghei probe or primer, Plasmodium berghei extrachromosomal genetic element and Plasmodium berghei. This phrase does not clearly define what the derived "nucleic acid" is as the source of the sample is not defined, the extrachromosomal element is not defined to be a plastid and may be any nucleic acid that is not chromosomally associated, the manner in which the nucleic acid is derived is not distinctly claimed, and the probe or primer is conserved in a malarial agent of humans, which is not Plasmodium berghei which infects rodents (rats and mice). Claims 2-11 and 13-15 are unclear based upon dependence upon claim 1.

Claim 2 defines the extrachromosomal genetic element to be a plastid or plastid-like molecule. Claim 2 defines the probe or prime to include the circular 35 kb molecule of Plasmodium berghei to be the highly conserved Plasmodium berghei and human malarial agent nucleic acid? The entire 35 kb molecule is not conserved with human malarial agents as the probe or primer would be the circular 35 kb molecule of Plasmodium berghei which is not a human pathogen, but a rodent pathogen. Clarification of what is intended by the claim limitations of claim 2 is requested.

Claim 3 recites the abbreviation "LSU". Abbreviations are definitely permitted in the claims upon their definition at their first appearance in the claims. Clarification is requested.

Claim 4 recites the phrase "wherein the probe or primer comprises an LSU rRNA gene or gene fragment that is highly conserved between Plasmodium berghei and the malarial agents of humans". The gene fragment is not defined to be a LSU gene fragment, but is a gene fragment that is highly conserved between Plasmodium berghei and the malarial agents of humans. The probe or primer comprises "a nucleotide sequence set forth in nucleotides 1147 to 1740 of SEQ ID NO 1. The phrase "a nucleotide sequence set forth in nucleotides" defines a genus of probes and primers that are subfragments of the recited sequences, to include a nucleotide sequence of any size sequence, as long as it comprises a conserved sequence, and is at least 15 nucleotides in length. What is the gene fragment that is being used as a probe or primer? Only functional characteristics are recited to define the recited structure. What the probe or primer is, is not distinctly claimed in light of the fact that Plasmodium parasites produce a plurality of genes that could comprise a shared nucleotide sequence with SEQ ID NO 1, nucleotides 1147 to 1740 and there is more than one plasmodium parasite for humans. See illustration below.

Reference sequence: SEQ ID NO 1147-1740 ----------

Claimed Probe or Primer: ??????????????????---???????????????????

Claim 4 recites the phrase "an LSU rRNA gene" depends from claim 3 which recites the phrase "plastid-localized LSU rRNA genes". Claim 4 is not further limiting of claim 3 as the

LSU rRNA gene of claim 4 is not required to be a plastid-localized LSU rRNA gene, but may be any LSU rRNA gene which could be chromosomally associated.

Claim 4 recites non-elected inventions; the elected invention is not distinctly claimed.

Claim 8 seeks to further limit claim 1 by defining the detection means. Claim 8 recites a methods step, a combination of structural components with specific relationships and a reporter molecule. The methods step is "identifying a signal produced", but the reporter molecule does not comprise a signal producing component, but must only be "capable of producing an identifiable signal". How can both conditions be true at the same time? One is a positive recitations of identifying something that exists, while the other statements sets forth a potential condition that may or may not exist. The claim is confusing because of the different tenses of words relative to the methods step recited in the claim. Clarification is requested.

Regarding claim 9, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 10 broadens the scope of claim 1 by defining the primers or primer pairs to be Plasmodium genus specific, and are not limited to the conserved sequences of the Plasmodium berghei probe or primer of claim 1. Claim 10 sets forth a combination of primers or primer pairs which is not the single probe or primer of claim 1. The genus specific primers or primer pairs are not defined to be Plasmodium berghei sequences that are detection agents for a human malarial agents. Plasmodium berghei is not human malarial agent and would not necessarily define a

source for genus specific primers or primer pairs for detecting human malarial agents. The functional limitations of claim 10 do not clearly set forth the claimed genus of primers and primer pairs that are specific across a plurality of genes, over a plurality of Plasmodial malarial pathogens. The invention of claim 10 appears to not include the probe or primer of Plasmodium berghei of claim 1; the invention is not distinctly claimed.

Claim 11 recites the phrase "wherein the PCR format comprises RT-PCR". What is being amplified? The probe or primer have not been defined to be an RNA or rRNA probe or primer. It is not clear how the RT-PCR functions in the claimed PCR format that does not set forth an RNA reagent.

Claim 13 recites the phrase "selected from the list consisting of". Markush language is "selected from the group consisting of".

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. (Generic claims) Claims 1-2, 5-7, 8-10, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ayyanathan et al (1996).

Ayyanathan et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in humans in a biological sample, the method comprising the steps of:

contacting a probe (see page 274, col. 1, Figure 1, narrative and nucleotide sequence) or primer (primer pair, see page 275, col. 1, first paragraph) that is found in an extrachromosomal genetic element (see page 273, key words; page 276, col. 2, Results and discussion first paragraph), and is also present and derived from Plasmodium berghei (see page 276, col. 2, Results and Discussion, first paragraph) with a biological sample (blood sample, see page 275, col. 1, preparation of DNA, paragraph 1) under stringent conditions (see page 277, col. 1, paragraph 2, line 5) ; and

detecting hybridization with the probe (see figure 2, page 274, and narrative for figure) or primer (see figure 5, page 277, top of page, and narrative) that is at least 15 nucleotides in length (21-120 nucleotides in length) and comprises a sequence that is highly conserved in Plasmodium berghei (see hybridization in figure 2, page 274) and in a human malarial agent (see Figure 2, page 274 and figure 5, for the detection of P.falciparum and P.vivax).

The sample was human blood. The probe and primers were conserved in P.berghei, as well as P.falciparum and P.vivax. The samples were detected by means of PCR , Northern or Southern blotting. The reference discloses the instantly claimed invention.

12. (Generic claims) Claims 1, 5-8, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al (US Pat. 4,707,445).

McCutchen et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in humans in a biological sample, the method comprising the steps of:

contacting a probe or a nucleic acid derived from Plasmodium berghei (see col. 3, lines 60-68 and col. 4, lines 1-16) with a biological sample; and

detecting hybridization with the probe or primer that is at least 15 nucleotides in length and comprises a sequence that is highly conserved in Plasmodium berghei (see col. 4, lines 11-16).

The reference discloses the instantly claimed invention.

13. (Generic claims) Claims 1, 5-9, 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al, (Science, 1984).

McCutchen et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood sample (see page 808, col. 3, middle to bottom half of paragraph, isolated parasites from host erythrocytes) with a probe or a nucleic acid derived from Plasmodium berghei (see page 810, Figure 2, narrative last three lines, probe is ribosomal gene probe, radio-labeled); and

detecting hybridization with a probe (see page 810, col. 3, paragraph 2, hybridized with radio labeled probe by Southern blot) that is at least 15 nucleotides in length and comprises a sequence that is highly conserved in Plasmodium berghei (see Table 1, gene hybridization with P.berghei, and falciparum).

The hybridization conditions were of a stringency that was low, moderate and high until hybridization was restricted to only one or two parasite DNA's (see page 810, col. 3, paragraph 2, middle of paragraph).

The reference anticipates the instantly claimed invention.

14. (Generic claims) Claims 1, 5-6 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by McCutchan et al, (1988, Molecular and Biochemical parasitology).

McCutchen et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood sample (see page 64, col. 2, paragraph 2,blood stage isolated parasites from host erythrocytes) with probe or a nucleic acid derived from Plasmodium berghei see Figure 3, page 66, col. 2, genus specific probe hybridization with P.berghei, P.falciparum); and

detecting hybridization with a probe (see page 66, hybridized with radio-labeled probe by Southern blot) that is at least 15 nucleotides in length and comprises a sequence that is highly conserved in Plasmodium berghei (see Figure 3, sequence, narrative, page 66, P.berghei, and falciparum).

McCutchan et al (1988) discloses the utilization of a P. Berghei small subunit rRNA probe for the hybridization and visualization of P.falciparum rRNA in a sample (see page 64, col. 1, paragraph 1), and shows a genus specific probe TM10 to hybridize with P.berghei, and P. falciparum (see Figure 3, page 66, col. 2). The reference anticipates the instantly claimed invention.

15. (Generic claims) Claims 1, 5-9, 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Das et al, (Analytical Biochemistry, 1996).

Das et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood sample (see page 262, col. 2, materials and methods, paragraph 1; isolated parasites from host erythrocytes) with a Plasmodium genus specific probe that hybridized to DNA derived from Plasmodium berghei (see page 263, Figure 1, Table 1, probe TM10, genus specific probe, radio labeled with P^{32} (see page 263, col. 1, paragraph 2); and

detecting hybridization with a probe (see Figures 1-3, especially figure 3, page 264, col. 1, bottom of page) that is at least 15 nucleotides in length and comprises a sequence that is highly conserved in Plasmodium berghei (see use of genus specific ribosomal probe).

The blood derived sample was dried on a positively charged nylon membrane (see page 262, col. 2, paragraph 3) prior to analysis. The reference anticipates the instantly claimed invention.

16. (Generic claims) Claim 1, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1994)

Gardner et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a sample (see page 307, col. 2, figure 1) with a human Plasmodium specific primer that hybridized to trn gene DNA, the primer being one that comprising a sequence that is conserved (see page 308, Figure 2 narrative shows PCR primers); and

detecting hybridization with a primer (see page 307, col. 2, paragraph 1, and Figure 1 narrative) that is at least 15 nucleotides in length, wherein the human derived primer successfully detected a human malarial agent.

The reference anticipates the instantly claimed invention.

17. (Generic claims) Claims 1-3, 5-10, 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Obst et al, (1990, Histochemistry).

Obst et al disclose the claimed invention directed to a method of detecting a Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a blood sample with a Plasmodium berghei probe that comprises a LSU rRNA nucleic acid sequence (see page 102, col. 1, paragraph 2, probe pPbSL7.8), wherein the probe hybridized to DNA in the sample (see page 102, col. 2, paragraph 3, signal produced

through biotin labeling (see page 102, col. 2, paragraph 3; page 103, col. 1-2 Discussion section and all frames of figure 1); to permit

detecting hybridization (the conditions were varied to obtain optimum hybridization, see page 101, col. 2, paragraph 3, last line). The probe was at least 15 nucleotides in length (7.8 kb, see page 102, col. 1, paragraph 2) and comprises a sequence that is highly conserved in Plasmodium berghei as the sequence was derived from Plasmodium berghei and comprises the coding sequence for the small ribosomal RNA and a portion of the large rRNA genes.

The blood derived sample was a blood smear that was dried prior to analysis (see page 101, col. 2, material and methods, paragraph 2). The reference anticipates the instantly claimed invention.

18. (elected species) Claims 1, 3-4, 8-9, 10, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al (1993, Nucleic acid research).

Please Note: In light of the P.berghei conserved sequence being any portion of SEQ ID No 1, nucleotides 1147 to 1740, the following rejection is being made of record as Gardner et al disclose a highly conserved, LSU rRNA Plasmodium nucleotide sequence "A/U", the complement of which was incorporated into a primer for the detecting of a human malarial agent in a biological sample.

Gardner et al disclose the claimed invention directed to a method of detecting a human Plasmodium malarial agent in a biological sample, the method comprising the steps of:

contacting a biological sample with a probe or primer (see DNA analysis section, page 1067, col. 2; page 1070, col. 1, first three lines define the most conserved positions and Table 1, col. 2; Figure 4) that comprises a LSU rRNA nucleic acid sequence of SEQ ID NO 1, nucleotides 1147-1740 that is conserved (complementary to "A/U", see page 1068, col. 1, paragraph 3) and found in an extrachromosomal element circular DNA that is a plastid (see sequence alignment) of a human malarial agent, wherein the probe or primer hybridized to DNA from a human malarial agent in the sample (see Figure 4, page 1070); to permit

detecting hybridization (see page 1070, figure 4), wherein the probe was at least 15 nucleotides in length (see page 1067, materials and methods, DNA analysis section and sequence alignment for X61660 and Figure 4, image and narrative).

The reference does not identify the sequence as being from P.berghei, but Gardner et al at page 1068, col. 1, paragraph 3, middle of paragraph, discloses a highly conserved sequence of P.falciparum, "A/U". The extremely conserved sequence was disclosed, and the complement thereof was incorporated into a primer for detecting a Plasmodial malarial agent of human in a biological sample and the primer comprised a highly conserved sequence for P.berghei (see sequence alignment of X61660).

The primer hybridized with a complementary sequence T/A (see primers disclosed on page 1067, col. 2, paragraph 1). The primer detected the presence of human Plasmodial agent P.falciparum DNA in a biological sample.

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

Conclusion

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

20. Clough et al (US Pat. 6,268, 160) is cited to show a method of screening for anti-malarial compounds.

21. Fichera et al (Nov. 1997) is cited to show guidance for drug targeting of malarial plastids in treatment of disease.

22. Gardner et al (1991, cited on Applicant's US-PTO1449) is cited to show both the SSU rRNA and LSU rRNA DNAs having been isolated.

23. Janse et al (1994) is cited to show the location of various genes in P.berghei, to include SSU rRNA and EF-tu.

24. Krungkrai, J et al (1993) is cited to show P.berghei cytochrome C oxidase.

25. Preiser, P et al (1995) is cited to show P.falciparum tRNA associated with a plastid-like extrachromosomal structure.

26. Rogers et al (US Pat. 6,313,090) is cited to show a method of treating parasitic infection.

27. Shaw et al (1996) is cited to show an anti-sense rRNA probe that recognizes all forms of small subunit rRNA present in P. Berghei, and also discloses P.berghei s21-mRNA.

28. Snounou et al (1992) is cited to show gene probes for P.berghei and other rodent malarial parasites.

29. Wataya et al (US Pat. 5,792,609) is cited to show detection of malaria utilizing primers.

30.Weissig et al (1997) is cited to show the utilization of SSU rRNA of P.falciparum 35 kb extrachromosomal element as a probe.

31.Wilson et al (1996, reference cited by Applicant in their US PTO 1449) is cited to show a method of detecting a human malaria agent utilizing the rpoB gene, the probe being non-radioactive, but fluorescent.

32. Yap et al (October 1997) is cited to show a partial nucleic acid sequence for the extrachromosomal plastid-like DNA of P.berghei.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
December 12, 2002

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